CLAIMS

1. A chimeric protein derived from a high-threshold calcium channel, characterized in that it comprises at least one β subunit or a fragment thereof including at least the BID domain, fused, at its NH_2 or COOH end, with the I-II loop of an α_1 subunit or a fragment thereof including at least the AID domain.

2. The chimeric protein as claimed in claim 1, characterized in that it consists of a β subunit fused, at its NH_2 or at its COOH end, with the I-II loop of an α_1 subunit.

3. The chimeric protein as claimed in claim 1, characterized in that it consists of the GK-like domain of a β subunit fused, at its NH_2 or COOH end, with the I-II loop of an α_1 subunit.

4. The protein as claimed in any one of claims 1 to 3, characterized in that the β subunit, or a fragment thereof, and the I-II loop, or a fragment thereof, are separated by a spacer peptide.

5. The chimeric protein as claimed in any one of claims 1 to 4, characterized in that it is derived from a G-protein-sensitive high-threshold calcium channel.

6. The chimeric protein as claimed in claim 5, characterized in that it comprises the I-II loop of an α_1 subunit selected from α_{1A}, α_{1B} and α_{1E}, or a fragment thereof.

7. The chimeric protein as claimed in any one of claims 1 to 6, characterized in that it comprises

a β subunit selected from the group consisting of β_1, β_2, β_3 and β_4, or a fragment thereof.

8. A variant chimeric protein derived from a chimeric protein as claimed in any one of claims 1 to 7, characterized in that it has a mutation of at least one amino acid in the sequences of said β subunit and/or of the I-II loop of an α_1 subunit.

9. The variant chimeric protein as claimed in claim 8, characterized in that said mutation modifies the affinity of the β subunit for the fragment of the I-II loop of the α subunit and/or vice versa.

10. The variant chimeric protein as claimed in claim 8 or claim 9, characterized in that said mutations are selected from the following mutations of the AID domain of the I-II loop of the α_1 subunit: Q383A, Q384A, E386D, E386S, L389H, G391R, Y392S, Y392F, W395A, I396A and E400A.

11. The chimeric protein as claimed in any one of claims 1 to 10, characterized in that it is coupled, preferably covalently, to at least one suitable label allowing the detection and/or the purification and/or the immobilization of said protein.

12. The chimeric protein as claimed in claim 11, characterized in that it comprises an acceptor or donor fluorophore respectively at its NH_2 and/or COOH end.

13. The chimeric protein as claimed in claim 12, characterized in that the acceptor fluorophore is the fluorescent protein CFP or BFP and the donor fluorophore is the fluorescent protein GFP or YFP.

14. A peptide, characterized in that it comprises a fragment of at least 7 amino acids of the sequence of the chimeric protein as claimed in any one of claims 1 to 13, located at the junction of the β subunit and of the I-II loop of the α_1 subunit of a calcium channel or of their fragments as defined in claim 1.

15. An antibody, characterized in that it is directed against a protein as claimed in any one of claims 1 to 13 or a peptide as claimed in claim 14.

16. A nucleic acid molecule, characterized in that it is selected from the group consisting of the sequences encoding a chimeric protein as claimed in any one of claims 1 to 13 or a peptide as claimed in claim 14, and the sequences complementary to the above sequences, that may be sense or antisense.

17. A probe and primer, characterized in that it comprises a sequence of approximately 10 to 30 nucleotides corresponding to that located at the junction of the β subunit and of the I-II loop of the α_1 subunit of a calcium channel or of their fragments as defined in claim 1.

18. A primer capable of amplifying the β subunit and/or the I-II loop of the α_1 subunit of a calcium channel or their fragments as defined in claim 1, characterized in that it is selected from the group consisting of the sequences SEQ ID NO: 1, 2, 4, 6, 7, 8 and 9.

19. A recombinant vector, characterized in that it comprises an insert selected from the group consisting of the nucleic acid molecules as claimed in claim 16.

20. The recombinant vector as claimed in claim 19, characterized in that it is a eukaryotic expression vector having a sequence selected from the group consisting of the sequences SEQ ID NO: 5 and SEQ ID NO: 10.

21. A cell modified with a recombinant vector as claimed in claim 19 or 20, with a nucleic acid molecules as claimed in claim 16 or with a chimeric protein as claimed in any one of claims 1 to 13.

22. The modified cell as claimed in claim 21, characterized in that it is a eukaryotic cell.

23. The modified cell as claimed in claim 21 or claim 22, characterized in that it expresses at least one receptor capable of coupling to G proteins.

24. A nonhuman transgenic mammal, characterized in that all or some of its cells are transformed with a nucleic acid molecule as claimed in claim 16.

25. The use of a product selected from the group consisting of the chimeric proteins as claimed in any one of claims 1 to 13, the nucleic acid molecules as claimed in claim 16, the recombinant vectors as claimed in claim 19 or claim 20, the modified cells as claimed in any one of claims 21 to 23 and the nonhuman transgenic mammals as claimed in claim 24, for studying the G-protein-coupled receptor-dependent cell signaling and regulatory pathways.

26. The use of a product selected from the group consisting of the chimeric proteins as claimed in any one of claims 1 to 13, the nucleic acid molecules as claimed in claim 16, the recombinant vectors as claimed in claim 19 or claim 20, the

modified cells as claimed in any one of claims 21 to 23 and the nonhuman transgenic mammals as claimed in claim 24, for screening agonists and/or antagonists of G-protein-coupled receptor-dependent cell signaling and regulatory pathways.

27. The use of a product selected from the group consisting of the chimeric proteins as claimed in any one of claims 1 to 13, the nucleic acid molecules as claimed in claim 16, the recombinant vectors as claimed in claim 19 or claim 20, the modified cells as claimed in any one of claims 21 to 23 and the nonhuman transgenic mammals as claimed in claim 24, for screening antagonists of the interaction between the α_1 and β subunits of high-threshold calcium channels.

28. A method for studying the G-protein-coupled receptor-dependent cell signaling and regulatory pathways, characterized in that it comprises at least the following steps:

a_1) culturing of modified cells expressing a chimeric protein derived from a G-protein-sensitive calcium channel and a G-protein-coupled receptor, as claimed in claim 23,

b_1) transduction of a signal via said G-protein-coupled receptor, by any appropriate means, and

c_1) determination, by any appropriate means, of the proportion of said chimeric protein expressed in said cells that is bound to a $G\beta\gamma$ subunit.

29. A method for screening agonists/antagonists of the G-protein-coupled receptor-dependent cell signaling and regulatory pathways, characterized in that it comprises at least the following steps:

a_2) culturing of modified cells expressing a chimeric protein derived from a G-protein-sensitive calcium channel and a G-protein-coupled receptor, as claimed in claim 23,

b_2) transduction of a signal via said G-protein-coupled receptor, by any appropriate means,

c_2) comparative determination, by any appropriate means, of the proportion of said chimeric protein expressed in the cells that is bound to a $G\beta\gamma$ subunit, before and after the bringing into contact of said cells in b_2) with a molecule to be tested, and

d_2) identification of the molecules that are agonists/antagonists of the G-protein-coupled receptor-dependent cell signaling and regulatory pathways, corresponding to those capable respectively of increasing and of decreasing the cellular concentration of free $G\beta\gamma$ subunits.

30. The method as claimed in claim 28 or claim 29, characterized in that said modified cells in a_1) or in a_2) express a chimeric protein coupled, at its NH_2 and COOH ends, respectively to a fluorescence donor fluorophore and a fluorescence acceptor fluorophore, and said determination in c_1) or in c_2) is carried out by means of the fluorescence transfer (FRET) technique.

31. A method for screening antagonists of the interaction between the α_1 and β subunits of high-threshold calcium channels, characterized in that it comprises at least the following steps:

a_3) bringing a molecule to be tested into contact with a chimeric protein derived from a G-

protein-sensitive or -insensitive calcium channel as claimed in any one of claims 1 to 13 and with a peptide comprising the AID domain of a G-protein-insensitive α_1 subunit,

b_3) measuring, by any appropriate means, the binding of said chimeric protein to said peptide, and

c_3) identifying the antagonists of the interaction between the α_1 and β subunits corresponding to those with which binding of said chimeric protein to said peptide is observed.

32. The screening method as claimed in claim 31, characterized in that said peptide comprising the AID domain is immobilized on a solid support and said chimeric protein is a chimeric protein as claimed in any one of claims 11 to 13.

33. A kit for implementing a method as claimed in any one of claims 28 to 32, characterized in that it comprises at least one product selected from the group consisting of the chimeric proteins as claimed in any one of claims 1 to 13, the nucleic acid molecules as claimed in claim 16, the recombinant vectors as claimed in claim 19 or claim 20, the modified cells as claimed in any one of claims 21 to 23 and the nonhuman transgenic mammals as claimed in claim 24.